(FILE 'HOME' ENTERED AT 14:03:19 ON 14 JAN 2003)

FILE 'MEDLINE, CANCERLIT, EMBASE, BIOSIS, BIOTECHDS' ENTERED AT 14:03:35
ON 14 JAN 2003

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L1        31218 S ANTHRACENE
L2        14148 S HYPERMUTA? OR MISMATCH REPAIR
L3           15 S L2 AND L1
L4            6 DUP REM L3 (9 DUPLICATES REMOVED)
L5        15224 S L1 NOT  (7,12-DIMETHYLBENZ[A]ANTHRACENE OR DMBA)
L6      8387880 S CELL#
L7         4861 S L6 AND L5
L8            2 S L7 AND L2
L9            2 DUP REM L8 (0 DUPLICATES REMOVED)
L10      802008 S MUTAT?
L11         267 S L10 AND L7
L12     3797568 S ASSAY OR IN VITRO OR CULTURED
L13         156 S L12 AND L11
L14          94 DUP REM L13 (62 DUPLICATES REMOVED)
L15          94 S L14 NOT  7-BROMOMETHYLBENZ(A)ANTHRACENE
L16          83 S L14 NOT  7-BROMOMETHYLBEN?
L17        3886 S MMR
L18           1 S L17 AND L1
L19       25812 S L1 NOT POLYCYCLIC
L20        1279 S L10 AND L19
L21         865 S L20 AND L6
L22         384 S L21 AND L12
L23         111 S L22 NOT  (7,12-DIMETHYLBENZ[A]ANTHRACENE OR DMBA)
L24          93 S L23 NOT 1,2-DIMETHY-9?

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L4 ANSWER 1 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002279209 EMBASE
TI Chemotherapeutic potential of curcumin for colorectal cancer.
AU Chauhan D.P.
CS D.P. Chauhan, Department of Medicine, University of California San Diego, 4028 Basic Science Building, La Jolla, CA 92093-0688, United States. dchauhan@ucsd.edu
SO Current Pharmaceutical Design, (2002) 8/19 (1695-1706).
Refs: 151
ISSN: 1381-6128 CODEN: CPDEFP
CY Netherlands
DT Journal; General Review
FS 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
052 Toxicology
LA English
SL English
AB Colorectal cancer is one of the leading causes of cancer deaths in the Western world. More than 56,000 newly diagnosed colorectal cancer patients die each year in the United States. Available therapies are either not effective or have unwanted side effects. Epidemiological data suggest that dietary manipulations play an important role in the prevention of many human cancers. Curcumin the yellow pigment in turmeric has been widely used for centuries in the Asian countries without any toxic effects. Epidemiological data also suggest that curcumin may be responsible for the lower rate of colorectal cancer in these countries. Curcumin is a naturally occurring powerful anti-inflammatory medicine. The anticancer properties of curcumin have been shown in cultured cells and animal studies. Curcumin inhibits lipooxygenase activity and is a specific inhibitor of cyclooxygenase-2 expression. Curcumin inhibits the initiation of carcinogenesis by inhibiting the cytochrome P-450 enzyme activity and increasing the levels of glutathione-S-transferase. Curcumin inhibits the promotion/progression stages of carcinogenesis. The anti-tumor effect of curcumin has been attributed in part to the arrest of cancer cells in S, G2/M cell cycle phase and induction of apoptosis. Curcumin inhibits the growth of DNA **mismatch repair** defective colon cancer cells. Therefore, curcumin may have value as a safe chemotherapeutic agent for the treatment of tumors exhibiting DNA **mismatch repair** deficient and microsatellite instable phenotype. Curcumin should be considered as a safe, non-toxic and easy to use chemotherapeutic agent for colorectal cancers arise in the setting of chromosomal instability as well as microsatellite instability.

L4 ANSWER 2 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002358978 EMBASE
TI Mice defective in the **mismatch repair** gene Msh2 show increased predisposition to UVB radiation-induced skin cancer.
AU Meira L.B.; Cheo D.L.; Reis A.M.; Claij N.; Burns D.K.; Te Riele H.; Friedberg E.C.
CS E.C. Friedberg, Department of Pathology, Southwestern Medical Center, University of Texas, Dallas, TX 75235, United States. friedberg.errol@pathology.swmed.edu
SO DNA Repair, (1 Nov 2002) 1/11 (929-934).
Refs: 22
ISSN: 1568-7864 CODEN: DRNEAR
PUI S 1568-7864(02)00143-X
CY Netherlands
DT Journal; Article

FS 016 Cancer
022 Human Genetics
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB Mice defective in the **mismatch repair** (MMR) gene Msh2 manifest an enhanced predisposition to skin cancer associated with exposure to UVB radiation. This predisposition is further heightened if the mice are additionally defective for the nucleotide excision repair gene Xpc. To test the hypothesis that the predisposition of Msh2 mutant mice to skin cancer reflects a mutator phenotype associated with increased proliferation of skin cells following exposure to UV radiation, Msh2 mutant mice were exposed to the tumor promoter TPA. Such mice showed a robust proliferative response in the skin, but did not manifest evidence of dysplasia or neoplasia. We conclude that the predisposition of Msh2 mice to UVB radiation-induced skin cancer reflects an interaction between the processes of **mismatch repair** and some other excision repair mode, the exact nature of which remains to be established.

L4 ANSWER 3 OF 6 MEDLINE DUPLICATE 1
AN 1999176825 MEDLINE
DN 99176825 PubMed ID: 10078939
TI Microsatellite instability during the immortalization and transformation of human breast epithelial cells in vitro.
AU Huang Y; Bove B; Wu Y; Russo I H; Yang X; Zekri A; Russo J
CS Breast Cancer Research Laboratory, Fox Chase Cancer Center, Philadelphia, Pennsylvania 19111, USA.
NC RO1 CA 67238 (NCI)
SO MOLECULAR CARCINOGENESIS, (1999 Feb) 24 (2) 118-27.
Journal code: 8811105. ISSN: 0899-1987.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
ED Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990331
AB The objective of this study was to determine whether microsatellite instability (MSI) and loss of heterozygosity (LOH) are involved in the immortalization of human breast epithelial cells (HBECs) in vitro and in the early stages of their transformation by benzo[a]pyrene (BP) and 7,12-dimethylbenz[a]**anthracene** (DMBA). We performed a genome-wide analysis of a total of 466 microsatellite DNA polymorphism loci along the X chromosome and the 22 pairs of human autosomes. MSI was found in the immortalized MCF-10F cells at the following loci: D11S1392 (on chromosome 11p13) and D17S849 (at 17p13.3), D17S796 (at 17p13.1), D17S513 (at 17p13.1), TP53 (at 17p13.1), D17S786 (at 17p13.1), and D17S520 (at 17p12) on chromosome 17. The BP-transformed cells exhibited MSI in the same loci and also in locus D11S912 (at 11q25). The more transformed BP1E cells also exhibited MSI on chromosome 13q12-13 at D13S260 and D13S289, markers known to flank the breast cancer susceptibility gene BRCA2. In the DMBA-transformed D3 and D3-1 cells, MSI was observed at the locus D13S260 in addition to the previously reported locus D16S285 (at 16q12.1). No LOH was observed on any of the chromosomes tested in these cells. These observations led us to conclude that the immortalization and transformation of HBECs may involve defects in mechanisms responsible for the cell's genomic stability, such as DNA replication and DNA **mismatch repair**.

L4 ANSWER 4 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1999031687 EMBASE
TI Transgenic systems in studies on genotoxicity of alkylating agents: Critical lesions, thresholds and defense mechanisms.
AU Kaina B.; Fritz G.; Ochs K.; Haas S.; Grombacher T.; Dosch J.; Christmann M.; Lund P.; Gregel C.M.; Becker K.
CS B. Kaina, Division of Applied Toxicology, Institute of Toxicology, University of Mainz, Obere Zahlbacher Str. 67, D-55131 Mainz, Germany
SO Mutation Research - Fundamental and Molecular Mechanisms of Mutagenesis, (1998) 405/2 (179-191).
Refs: 77
ISSN: 0027-5107 CODEN: MRFMEC
PUI S 0027-5107(98)00135-3
CY Netherlands
DT Journal; Conference Article
FS 016 Cancer
022 Human Genetics
052 Toxicology
LA English
SL English
AB Transgenic systems, both cell lines and mice with gain or loss of function, are being used in order to modulate the expression of DNA repair proteins, thus allowing to assess their contribution to the defense against genotoxic mutagens and carcinogens. In this review, questions have been addressed concerning the use of transgenic systems in elucidating critical primary DNA lesions, their conversion into genotoxic endpoints, low-dose effects, and the relative contribution of individual cellular functions in defense. It has been shown that the repair protein alkyltransferase (MGMT) is decisive for protection against methylating and chloroethylating compounds. Protection pertains also to tumor formation, as revealed by the response of MGMT transgenic and knockout mice. Overexpression of genes involved in base excision repair (N-methylpurine-DNA glycosylase, apurinic endonuclease, DNA polymerase .beta.) is in most cases not beneficial in increasing the protection level, whereas their down-modulation or inactivation increases cellular sensitivity. This indicates that non-repaired base N-alkylation lesions and/or repair intermediates possess genotoxic potential. Modulation of **mismatch repair** and poly(ADP)ribosyl transferase has also been shown to affect the cellular response to alkylating agents. Furthermore, the role of Fos, Jun and p53 in cellular defense against alkylating mutagens is discussed. Copyright (C) 1998 Elsevier Science B.V.

DUPLICATE 2

L4 ANSWER 5 OF 6 MEDLINE
AN 96173957 MEDLINE
DN 96173957 PubMed ID: 8597530
TI Microsatellite instability and loss of heterozygosity on chromosome 10 in rat mammary tumors induced by 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine.
AU Toyota M; Ushijima T; Weisburger J H; Hosoya Y; Canzian F; Rivenson A; Imai K; Sugimura T; Nagao M
CS Carcinogenesis Division, National Cancer Center Research Institute, Tokyo, Japan.
SO MOLECULAR CARCINOGENESIS, (1996 Mar) 15 (3) 176-82.
Journal code: 8811105. ISSN: 0899-1987.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199604
ED Entered STN: 19960506
Last Updated on STN: 19980206
Entered Medline: 19960424

AB Microsatellite instability (MI) and loss of heterozygosity (LOH) were examined in mammary tumors induced in Sprague-Dawley x F344 F1 female rats by 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP). Examination of 62 microsatellite loci revealed MI in nine of 15 (60%) PhIP-induced mammary tumors, and five of these MI-positive tumors had mutations in more than one microsatellite locus. In contrast, two of 12 (17%) 7,12-dimethylbenz[a]**anthracene** (DMBA)-induced mammary tumors were MI positive but had mutations at only one locus each. Further, by using 37 polymorphic markers specific LOH was observed in four of 15 PhIP induced mammary tumors on distal parts of rat chromosome 10, which is homologous to human chromosome 17q with no background level of LOH. Similarly, DMBA-induced mammary tumors showed specific LOH on the same region of chromosome 10. These data suggest that **mismatch-repair** deficiency and loss of chromosome 10 are involved in carcinogenesis of PhIP-induced rat mammary tumors.

DUPLICATE 3

L4 ANSWER 6 OF 6 MEDLINE
AN 81098342 MEDLINE
DN 81098342 PubMed ID: 6935492
TI Defective excision repair in a mutant of Micrococcus radiodurans **hypermutable** by some monofunctional alkylating agents.
AU Tempest P R; Moseley B E
SO MOLECULAR AND GENERAL GENETICS, (1980) 179 (1) 191-9.
Journal code: 0125036. ISSN: 0026-8925.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198103
ED Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19810324

AB The lethal and mutagenic effects of methyl methanesulphonate (MMS), ethyl methanesulphonate (EMS), and N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) can be dissociated in a mitomycin C (MTC)-sensitive mutant, strain 302, of Micrococcus radiodurans. As regards lethality 302 is extremely sensitive, compared with the wild type, to MTC and decarbamoyl MTC (DCMTC), slightly sensitive to EMS, MNNG, nitrous acid, 7-bromomethylbenz[alpha] **anthracene** (BrMBA), and N-acetoxy-N-2-acetylaminofluorene (AAAF), and resistant to MMS, hydroxylamine, and ICR 191G. As regards mutability it is, compared to the wild type, very sensitive to MMS, EMS, and MNNG, and slightly sensitive to hydroxylamine and nitrous acid but not to any other agent examined. Alkaline sucrose gradient studies indicate the 302 does not incise DNA containing BrMBA adducts, although it does incise DNA damaged by AAAF but probably not to the same extent as wild type. We put forward the hypothesis that the **hypermutability** of 302 is due to the non-removal of bases or nucleotides, modified in exocyclic positions, which have altered base-pairing capabilities, while lethality results from the non-removal of bases or nucleotides, also modified in exocyclic positions, which no longer form hydrogen-bonded base pairs.

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L14 ANSWER 94 OF 94 CANCERLIT
AN 73701234 CANCERLIT
DN 73701234
TI THE INDUCTION OF AZAGUANINE-RESISTANT MUTANTS IN **CULTURED** CHINESE HAMSTER **CELLS** BY REACTIVE DERIVATIVES OF CARCINOGENIC HYDROCARBONS.

AU Duncan M E; Brookes P
CS Chem. Carcinogenesis Div., Chester Beatty Res. Inst., London, England.

SO Mutat Res, (1973) 21 (2) 107-118.
ISSN: 0027-5107.

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Assessment Review Committee
EM 197512
ED Entered STN: 19941107
Last Updated on STN: 19941107

AB 7-Bromdethylbenz(a)**anthracene** (7-BrMeBA), a weak carcinogen, and 7-bromomethyl-12-methylbenz[a]**anthracene** (7-BrMe12MeBA), an active carcinogen, were tested for their abilities to induce azaguanine-resistant mutants in azaguanine-sensitive V79 Chinese hamster **cell** cultures. Sensitive **cells** grown for 15 min in medium containing one of the carcinogens were recultured and azaguanine was added at different times. The induced **mutation** frequency increased arithmetically with the number of **cell** divisions which occurred following exposure to carcinogen and prior to addition of azaguanine, and reached a maximum after three or four divisions. The percentage of induced **mutations** declined sharply when **cells** were allowed to progress beyond four divisions. At a given concentration, 3H-labeled 7-BrMeBa, the weaker carcinogen, bound five times more extensively to cellular DNA and RNA than did 7-BrMe12BA. At low doses both compounds gave a similar linear **mutation** response with a slope of about 5 x 10-5 induced mutants/ survivor/micromole hydrocarbon bound/mole of DNA phosphorus. However, at extents of DNA binding greater than 8micromoles mole phosphorus, 7-BrMeBA was much more mutagenic than 7-BrMe12BA. These data were consistent with the existence of two distinct mechanisms for the induction of mutants by these two hydrocarbon derivatives.

DUPLICATE 33

L14 ANSWER 83 OF 94 MEDLINE

AN 77206380 MEDLINE

DN 77206380 PubMed ID: 873646

TI The metabolic activation of 7-methylbenz(a)**anthracene**: the induction of malignant transformation and **mutation** in mammalian **cells** by non-K-region dihydrodiols.

AU Marquardt H; Baker S; Tierney B; Grover P L; Sims P

SO INTERNATIONAL JOURNAL OF CANCER, (1977 Jun 15) 19 (6) 828-33. Journal code: 0042124. ISSN: 0020-7136.

CY Denmark

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 197708

ED Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19770812

AB Four different dihydrodiols derived from 7-methylbenz(a)**anthracene** have been tested, together with the parent hydrocarbon, for their ability to induce the in **vitro** malignant transformation of mouse M2 fibroblasts and **mutations** in V79 Chinese hamster **cells** . In the transformation tests withe the non-K-region dihydrodiols, the 3,4-diol was the most active dihydrodiol tested and the 8,9-diol was also more active than 7-methylbenz(a)**anthracene** itself; the 1,2-diol showed only slight activity. The K-region dihydrodiol, the 5,6-diol, which cannot be directly metabolized to a vicinal diol-epoxide, was inactive. These differences in biological activity were similar to those apparent in the results from the mutagenicity tests. The data support the general hypothesis that non-I-region dihydrodiols, which can be metabolized to vicinal diol-epoxides, are important in the metabolic activation of the carcinogenic polycyclic hydrocarbons and, when taken together with other results, indicate that 3,4-dihydro-3,4-dihydroxy-7-methylbenz(a) **anthracene** is most probably involved in the metabolic activation of 7-methylbenz(a)**anthracene** presumably following conversion into the related diol-epoxide, 3,4-dihydro-3,4-dihydroxy-7-methylbenz(a) **anthracene** 1,2,-oxide.

L14 ANSWER 80 OF 94 MEDLINE

AN 78167194 MEDLINE

DN 78167194 PubMed ID: 647680

TI Carcinogenicity and mutagenicity of benz(a)**anthracene** diols and diol-epoxides.

AU Slaga T J; Huberman E; Selkirk J K; Harvey R G; Bracken W M

SO CANCER RESEARCH, (1978 Jun) 38 (6) 1699-704.
Journal code: 2984705R. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 197807

ED Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19780726

AB Benz(a)**anthracene** (BA) and its five possible trans-dihydrodiols were evaluated for determination of their skin tumor-initiating activity and their mutagenic activity in Chinese hamster V79 **cells**. In addition, the skin tumor-initiating abilities of five diol-epoxides of BA were tested. Results showed (+/-)-trans-3,4-dihydroxy-3,4-dihydrobenz(a)**anthracene** (BA 3,4-dihydrodiol) to be approximately 10 times more mutagenic than was BA and about 20 times more mutagenic than were the other possible dihydrodiols in the V79 **cells** cocultivated with irradiated hamster embryo **cells**. As a skin tumor initiator, BA 3,4-dihydrodiol was approximately 5 times more active than BA, whereas the other BA dihydrodiols were all less active tumor initiators. (+/-)-trans-3alpha,4beta-Dihydroxy-1alpha,2alpha-epoxy-1,2,3,4-tetrahydrobenz(a)**anthracene** was found to be approximately 20% more active as a tumor initiator than was BA 3,4-dihydrodiol, whereas the other diol-epoxides of BA were less active than BA itself. The results suggest that the bay-region diol-epoxide of BA may be the ultimate carcinogen and mutagenic form of BA.

L16 ANSWER 23 OF 83 MEDLINE
AN 86189473 MEDLINE
DN 86189473 PubMed ID: 3754483
TI Benz[a]**anthracene**-induced alterations in the metabolic activation of benzo[a]pyrene by hamster embryo **cell** cultures.

AU Smolarek T A; Moynihan C G; Salmon C P; Baird W M
NC CA-28825 (NCI)
SO CANCER LETTERS, (1986 Mar) 30 (3) 243-9.
Journal code: 7600053. ISSN: 0304-3835.

CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198605
ED Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860530

AB Co-administration of benz[a]**anthracene** (BA) with benzo[a]pyrene (B[a]P) to hamster embryo **cell** cultures for 24 h resulted in a decrease in the metabolism of benzo[a]pyrene by 40%, a decrease in the level of binding of B[a]P to DNA by 70% and a 10-fold reduction in **mutation** induction in a hamster embryo **cell**-mediated V79 **cell mutation assay**. This data indicates that the biological effects of co-administration of BA with B[a]P result from inhibition of the metabolic activation of B[a]P rather than induction of enzymes that detoxify the B[a]P.

cancer.

L16 ANSWER 9 OF 83 MEDLINE
AN 1998178689 MEDLINE
DN 98178689 PubMed ID: 9519874
TI A transgenic mouse model for mammary carcinogenesis.
AU Li B; Murphy K L; Laucirica R; Kittrell F; Medina D; Rosen J M
CS Hughes Institute, Roseville, Minnesota 55113, USA.
NC CA16303 (NCI)
GM08231 (NIGMS)
SO ONCOGENE, (1998 Feb 26) 16 (8) 997-1007.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980410
Last Updated on STN: 19980410
Entered Medline: 19980402

AB Missense **mutations** in the p53 tumor suppressor occur frequently in human breast cancer and influence both the prognosis and response to chemotherapy. Amino acid 175 (equivalent to murine 172) is the second most common site of missense **mutations** in p53 in human breast cancer. Over 95% of these **mutations** are arginine-to-histidine (R-H) substitutions resulting in a gain-of-function, and not merely a dominant-negative phenotype. Transgenic mice expressing a p53 172(R-H) construct targeted to the mammary gland by means of a whey acidic protein (WAP) promoter were characterized as a model system in order to determine the specific effects of this **mutation** on mammary tumorigenesis. Although transgene expression alone had no apparent effect on normal mammary development, transgenic mice treated with the chemical carcinogen dimethylbenz(a)**anthracene** developed tumors with much shorter latency than did control littermates and had a greater tumor burden. Tumors arising in transgenic mice did not exhibit either decreased apoptosis or increased **cell** proliferation relative to tumors arising in nontransgenic littermates, but did display increased genomic instability. Large pleiomorphic nuclei were visible in many tumors from transgenic mice, and DNA flow analysis confirmed the presence of significant aneuploid **cell** populations. Since these transgenic mice develop very few spontaneous tumors, while accelerating carcinogen-and oncogene-mediated tumorigenesis, this mouse model will, therefore, be useful in the investigation of early events in mammary tumorigenesis. It may also be used as a preclinical model to test newly developed chemotherapeutic strategies.

L16 ANSWER 7 OF 83 MEDLINE

AN 1998404139 MEDLINE

DN 98404139 PubMed ID: 9733500

TI **Anthracene**-9,10-diones as potential anticancer agents: bacterial **mutation** studies of amido-substituted derivatives reveal an unexpected lack of mutagenicity.

AU Venitt S; Crofton-Sleigh C; Agbandje M; Jenkins T C; Neidle S

CS Section of Molecular Carcinogenesis and Cancer Research Campaign Biomolecular Structure Unit, The Institute of Cancer Research, Royal Cancer Hospital, Sutton, Surrey SM2 5NG, UK.

SO JOURNAL OF MEDICINAL CHEMISTRY, (1998 Sep 10) 41 (19) 3748-52. Journal code: 9716531. ISSN: 0022-2623.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199810

ED Entered STN: 19981020
Last Updated on STN: 19981020
Entered Medline: 19981008

AB Fifteen **anthracene**-9,10-dione ("anthraquinone") derivatives with (omega-aminoalkyl)carboxamido substituents at the 1-, 2-, 1,4-, or 2,6-ring positions were tested for bacterial mutagenicity in reverse-**mutation** assays using Salmonella typhimurium frameshift strains TA1538, TA98, and TA97a, in the presence and absence of a metabolic activation system prepared from the livers of rats treated with Aroclor 1254. Six of the compounds were also tested in S. typhimurium TA100 and Escherichia coli WP2uvrApKM101 strains, which carry **mutations** particularly sensitive to reversion by DNA base-pair substitution. Two structurally related compounds, mitoxantrone and bisantrene, were tested in parallel as positive controls. Mitoxantrone was mutagenic to S. typhimurium TA1538 and TA98, whereas bisantrene was weakly mutagenic to both these strains but strongly mutagenic toward the TA97a variant. By contrast, although they are also DNA-binding intercalators, none of the amide-functionalized **anthracene**-9,10-diones of the present study showed significant mutagenic activity in any of the bacterial strains examined. Further, neither substituent position nor systematic alterations in the nature of attached side chains appeared to induce mutagenicity with these agents, although other studies have shown that such structural factors markedly influence their cytotoxic potencies toward mammalian **cells** in **vitro**.

L24 ANSWER 18 OF 93 MEDLINE
AN 89168222 MEDLINE
DN 89168222 PubMed ID: 2647293
TI Influence of the alkyl substituent on mutagenicity and covalent DNA binding of bay region diol-epoxides of 7-methyl- and 7-ethylbenz(a) **anthracene** in Salmonella and V79 Chinese hamster **cells**.
AU Glatt H; Harvey R G; Phillips D H; Hewer A; Grover P L
CS Department of Toxicology of the University, Mainz, Federal Republic of Germany.
NC CA-36097 (NCI)
SO CANCER RESEARCH, (1989 Apr 1) 49 (7) 1778-82.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198905
ED Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890505
AB The anti-isomers of the bay region diol-epoxides of the strong carcinogen 7-methylbenz(a)**anthracene** and of the weak carcinogen 7-ethylbenz(a)**anthracene** were investigated for mutagenicity in Salmonella typhimurium (reversion of the his - strains TA98 and TA100 to prototrophy) and V79 Chinese hamster **cells** (acquisition of resistance to 6-thioguanine and ouabain; formation of micronuclei). In addition, in the V79 **cells**, the levels of the DNA adducts formed were determined by 32P-postlabeling analysis. In terms of **mutations** per nmol compound administered, the methyl derivative was four to 10 times more potent, depending on the genetic endpoint, than its ethyl congener. However, when the results were expressed as **mutations** per adduct, the difference between the two diol-epoxides was small. Therefore, a higher level of DNA modification appears to be the major reason for the stronger mutagenicity of the methyl derivative. However, both diol-epoxides had similar half-lives (about 9 min) in physiological buffer, as determined from the decline in mutagenic activity after preincubation of the test compound. These results suggest that the effect of the 7-alkyl group on the extent of reaction with DNA is more a result of steric factors than of a change in the intrinsic chemical reactivity of the diol-epoxides.